REMARKS

Applicants submit this Amendment to indicate the insertion point for the substitute Sequence Listing filed concurrently herewith. Applicants respectfully request examination on the merits of this application.

Receipt of the initial Office Action on the merits is awaited.

Respectfully submitted,

10 January 2002
Date

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Versions with Markings to Show Changes Made

IN THE SPECIFICATION

Please replace the paragraphs beginning on page 7 at lines 3 and 7 with the following rewritten paragraphs, respectively:

FIG. 2 (SEQ ID NOS: 1-2, 92-94) Shows schematic representations of example intracellular targeting sequences for use with single chain monoclonal antibody reagents. Targeting vectors direct expression of sFvs to either the cytoplasm, nucleus, endoplasmic reticulum, or the mitochondria.

FIG. 3 (SEQ ID NO: 95) Shows the pBTM116 yeast expression plasmid as an example vector used to construct antigen (X) "bait" strain fusions to screen the antibody fusion reagent library.

Please replace the paragraph beginning on page 24 at line 27 with the following rewritten paragraph:

Preferred embodiments of the single chain monoclonal antibody fusion reagents consist of an antibody light chain variable domain (V_L) and heavy chain variable domain (V_H) connected by a short flexible linker, preferably a peptide (SEQ ID NO: 96) $[(Gly)_4Ser]_3$ which allows the molecule to assume a conformation that is capable of binding an antigen. Nicholls, PJ, Johnson, VG, Blanford, MD, Andrew, SM., J. Immunol. Methods, 165:81-91, 1993. Most preferably there is a short flexible linker between the two immunoglobulin variable domains, e.g., V_L – $[(Gly)_4Ser]_3$ – V_H or V_H - $[(Gly)_4Ser]_3$ V_L

Please replace the paragraph beginning on page 26 at lines 26 with the following rewritten paragraph:

Another embodiment of the present invention is nuclear expression for anti-transcription factor single chain monoclonal antibody fusion reagents. A nuclear-targeting version of an expression vector (FIG. 2) facilitates cloning of the immunoglobulin domain with 3 repeats of the nuclear localization signal (NLS) derived from SV40 T antigen (DPKKKRKV) (SEQ ID NO: 92) and a myc epitope tag at the C –terminus. Biocca, S, Nueberger, MS, Cattaneo, A Embo J. 1:101-108, 1990.

Please replace the paragraph beginning on page 27 at lines 8 with the following rewritten paragraph:

Targeting of single chain antibody fusion reagents of the present invention to the endoplasmic reticulum is a contemplated embodiment to prevent secretion of specific proteins. A presently available endoplasmic reticulum (ER) targeting vector allows for cloning of the antibody region in frame with a myc epitope tag followed by an ER retention signal (SEKDEL) (SEQ ID NO: 93). Munro, S, Pelham, RB. Cell 48:899-907, 1987. The utility of this embodiment is to prevent secretion of a Protein that is normally secreted by sequestration/neutralization and/or retaining the target/fusion reagent complex in the endoplasmic reticulum. Anti-erbB2 and anti-VEGF are embodiment fusion reagents to block secretion of a transmembrane protein (epidermal growth factor (EGF) receptor with anti-erbB2) and a secreted protein (vascular endothelial growth factor (VEGF) with anti-VEGF).

Please replace the paragraph beginning on page 34 at line 12 with the following rewritten paragraph:

The linkered variable region PCR products are generated using the appropriate primers that have been fused to a sequence that when overlapped with the homologous sequences from the other chain variable region product will encode the $[(Gly)_4Ser]_3$ (SEQ ID NO: 96) linker sequence between the two variable domains.